Future drugs from the sea

Several marine chemicals are likely candidates for future drugs. Here are a few being explored by US scientists.

- **Discodermolide** from the Bahamian sponge *Discodermia dissoluta* is a powerful immunosuppressive agent that may have a future role in suppressing organ rejection after transplant surgery.
- **Bryostatin** from the West Coast bryozoan (moss animal) *Bugula neritina* and **didemnin B** from a Caribbean tunicate of the genus *Tridemnum* are both in clinical trials as cancer treatments.
- **Pseudopterosin E** from the Caribbean gorgonian coral *Pseudopterogorgia elisabethae* and **scalaradial** from dictyoceratid sponges found in the western Pacific are both being studied as anti-inflammatory agents.
- **Dolasstatin** from the sea hare *Dolabella auricularia* and **ecteinascidin** from the tunicate *Ecteinascidia turbinata* have pending clinical trial application as anti-cancer compounds.
- **Halichondrin B** from the sponge *Lissodendoryx* (and others) and **halmon** from the red algae *Portieria hornemannii* have reached preclinical trial stage as anti-cancer compounds.

Other marine chemicals are being investigated in Europe and in Japan, but we know less about the progress of these studies. There appears to be no shortage of marine chemicals that are potential candidates for drugs. The problem is that so many chemicals show promising activity in the initial screens that it is very difficult to predict which will become truly significant discoveries.

It seems inevitable that economic considerations will prevent the development of many marine chemicals that are very effective but difficult to obtain. The rise and fall of interest in marine prostanoids clearly illustrates this. Prostaglandins are important human hormones that control blood pressure, renal blood flow, contractions of smooth muscle, and gastric acid secretion, and are involved in inflammation. When prostagladins were first isolated from sheep seminal tissues, these were difficult to obtain in even minute quantities and were extremely expensive. When closely related chemicals called prostanoids were acquired in substantial quantities from the Caribbean gorgonian coral *Plexaura homomalla*, there was a rush to harvest gorgonians, isolate the prostanoids, and convert these chemicals into biochemically active prostagladins. Within a year, however, prostagladins were being produced by laboratory synthesis, and the marine prostanoids were soon forgotten, much to the relief of those who value the shallow reef environment's natural beauty. This episode provided a valuable lesson for entrepreneurs seeking new pharmaceuticals

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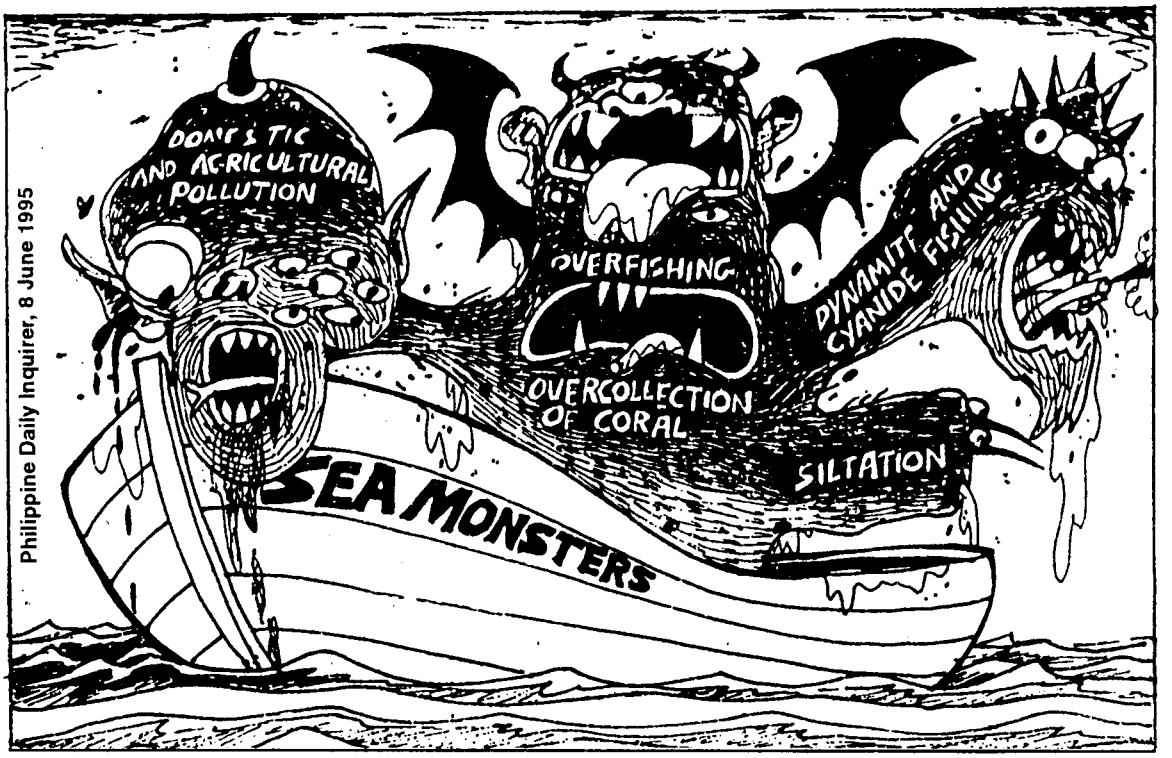
> The discovery of a new drug from an organism's molecular structure will not mean a mass harvesting of the oceans. Scientists will eventually culture the organism or synthesize its molecular structure in the laboratory.
>
> - Dr. Paul Scheuer, University of Hawaii
> **Makai** 15(7) July 1993



Philippine Daily Inquirer, 8 June 1995

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describes a potent poison found in seaweed known as **limu-make-O-Hana** (the deadly seaweed of Hana). The islanders of old smeared the tips of their lances. It was not until 1861 that the habitat described in the legend was discovered and scientists were able to collect the seaweed. Moore and Scheuer isolated the toxin in 1971, and its structure was definitively established ten years later. Palitoxin has an unusual structure. Despite its great molecular weight (around 3,300 daltons), it is not formed by the repetition of simple structural units like polysaccharides. Palitoxin is extremely poisonous (LD_{50} about 0.5 µg/kg in rats) and possesses antitumoral properties. A dose of around one-tenth of the minimum lethal dose completely cures Ehrlich's tumor in rats. It has recently been used as a local anaesthetic in maxillofacial surgery, allowing surgeons to operate for several hours at a time. It is a powerful vasoconstrictor and is potentially useful in the study of angina in animals.

Excerpted from: Luigi Minale. 1985. *Medicine from the sea.* In: SG Richardson (ed). **Managing the Ocean; Resources, Research, Law.** Lomond Publications Inc. Maryland 1985.

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from marine organisms: **We should expect marine chemicals to inspire new drugs rather than to provide them.**

Chemicals from marine organisms have proved to be different from plant sources, and have provided valuable tools for biomedical research, as well as inspiration to the pharmaceutical industry. Biochemical studies have positively influenced marine biology, in as much as they have focused attention on marine invertebrates and led to pioneering research on invertebrate aquaculture and invertebrate-cell tissue culture. If we consider the 1980s to be a period of basic research on chemicals from marine organisms, then the 1990s will surely see new drugs and other chemical products that are inspired by this research. We will then have accomplished our goal of demonstrating the biomedical potential of chemicals from marine organisms without causing any lasting damage to the marine environment.

Sources: (1) **Oceanus**, 1992. **Oceanus** reports on research at the Woods Hole Oceanographic Institution. (2) **Science** Vol. 266. November 25, 1994.